

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 March 2005 (03.03.2005)

PCT

(10) International Publication Number
WO 2005/018561 A3

(51) International Patent Classification⁷: **A61K 31/405**,
31/44, 31/535, C07D 209/04, 221/02, 415/00

(21) International Application Number:
PCT/US2004/026909

(22) International Filing Date: 20 August 2004 (20.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/496,639 20 August 2003 (20.08.2003) US
60/496,722 20 August 2003 (20.08.2003) US
60/496,810 21 August 2003 (21.08.2003) US
60/498,291 28 August 2003 (28.08.2003) US
60/498,308 28 August 2003 (28.08.2003) US
60/530,643 19 December 2003 (19.12.2003) US

(71) Applicant (for all designated States except US): **NITROMED, INC.** [US/US]; 125 Spring Street, Lexington, MA 02421 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GARVEY, David**, S. [US/US]; 10 Grand Hill Drive, Dover, MA 02030 (US). **LETTS, Gordon, L.** [AU/US]; 12 Abbott Road, Dover, MA 02030 (US). **WORCEL, Manuel** [FR/US]; 20 Gloucester Street No. 4, Boston, MA 02115 (US). **GASTON, Ricky, D.** [US/US]; 252 Kennedy Drive, No. 512, Malden, MA 02148 (US).

(74) Agents: **GRIEFF, Edward, D.** et al.; Wilmer Cutler Pickering Hale and Dorr LLP, The Willard Office Building, 1455 Pennsylvania Avenue, NW, Washington, DC 20004 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
21 July 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **NITROSATED AND NITROSYLATED CARDIOVASCULAR COMPOUNDS, COMPOSITIONS AND METHODS OF USE**

(57) Abstract: The invention describes novel nitrosated and/or nitrosylated cardiovascular compounds or pharmaceutically acceptable salts thereof, and novel compositions comprising at least one nitrosated and/or nitrosylated cardiovascular compound, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides novel compositions and kits comprising at least one cardiovascular compound of the invention, that is optionally nitrosated and/or nitrosylated, and, optionally, at least one nitric oxide donor compound and/or at least one therapeutic agent. The invention also provides methods for (a) treating cardiovascular diseases; (b) treating renovascular diseases; (c) treating diabetes; (d) treating diseases resulting from oxidative stress; (e) treating endothelial dysfunctions; (f) treating diseases caused by endothelial dysfunctions; (g) treating cirrhosis; (h) treating pre-eclampsia; (j) treating osteoporosis; and (k) treating nephropathy. The nitrosated and/or nitrosylated cardiovascular compounds are preferably nitrosated and/or nitrosylated P-adrenergic antagonists, nitrosated and/or nitrosylated angiotensin converting enzyme (ACE) inhibitors, nitrosated and/or nitrosylated anti-hyperlipidemic compounds, and nitrosated and/or nitrosylated antithrombotic and vasodilator compounds.

WO 2005/018561 A3